## REMARKS

### Claim Objections

The Examiner objected to claims 26-29 as being drawn to non-elected claim 22. Claims 26 and 27, as amended, depend from "claim 21 or claim 23" and, therefore, the objection has been obviated. This amendment to claim 27 also obviates the objection to claims 28 and 29, which depend from claim 27. Furthermore, none of the new claims depend from a non-elected claim or recite non-elected species.

### New Claims

Applicants have added new claims 38-42 to more clearly define the claimed methods. No new matter is introduced by new claims 38-42. Specifically, exemplary support for each new claim is presented in the following table.

| Claim | Support |
|---|---|
| 38 | Original claim 21; page 9, lines 8-20. |
| 39 | Original claim 26; page 5, lines 15-23. |
| 40 | Original claim 29; page 9, lines 1-4. |
| 41 | Page 9, lines 5-8. |
| 42 | Page 9, lines 5-8. |

### 35 U.S.C. § 112, first paragraph–Written Description

Claims 21, 23, and 26-29 were rejected under 25 U.S.C. § 112, first, paragraph as allegedly lacking adequate written description. According to the Examiner, those claims contain subject matter that was not described in the specification in such a way

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as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Specifically, the Examiner contends that

> [t]he specification only teaches two GM4,6D, SEQ ID NO:2 and 3. These two representative species is not enough to describe the whole genus and there is no evidence on the record of the relationship between the structure of SEQ ID NO:2 and 3 and the structure of a GM4,6D from another source. Therefore, the specification fails to describe other representative species of the genus of GM4,6D.

(Office Action at page 3.)

The fundamental factual inquiry in a written description rejection is whether the claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the written description requirement. M.P.E.P 2163.02. Rather, the inquiry into whether the written description requirement is met must be determined on a case-by-case basis and is a question of fact. *In re Wertheim*, 191 U.S.P.Q. 90, 96 (C.C.P.A. 1976). The Examiner has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in an Applicant's disclosure a description of the invention defined by the claims. *Id.* at 98; M.P.E.P 2163.04.

At the time that the application was filed, Applicants had possession of the claimed methods for treating a subject having an inflammatory disorder by administering modulators or inhibitors of the disclosed GM4,6D polypeptides. As stated above, the Examiner alleges that two sequences for GM4,6D are not sufficient to describe the

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genus of GM4,6D polypeptides. The Examiner's rejections suggest that Applicants are prosecuting composition claims directed to GM4,6D proteins, instead of methods of treating inflammatory diseases using agents that modulate the disclosed GM4,6D polypeptides. The Examiner appears to rely on *University of California v. Eli Lilly and Co.*, 43 U.S.P.Q. 2d 1398, 1406 (Fed. Cir. 1997) for the proposition that the sequence of two proteins does not provide written descriptive support for a genus of related proteins. This, however, is not a proper application of *Lilly* to this case. *Lilly* focused on composition claims and only stated that this stringent requirement applies to composition claims, DNA claims in particular. The law does not require the same information to satisfy the written description requirement for method claims—especially methods of affecting the protein in question.

Instead, in order to satisfy the written description requirement for a method claim, the specification must show that the method as a whole was within the possession of the inventors at the time of filing. The written description requirement is satisfied if the broader concept would naturally occur to one skilled in the art upon reading the earlier specification. *In re Smythe*, 480 F.2d 1376, 1384 (C.C.P.A. 1973).

Despite the Examiner's assertion otherwise, this application adequately discloses the claimed methods of treating inflammatory diseases that result from aberrant or excessive GM4,6D activity. Applicants submit that the focus of the inquiry should not be not whether Applicants have described every protein that can be used in the claimed methods, but whether Applicants have described the claimed methods.

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As the Examiner acknowledges, the application describes in both the actual chemical structure and the functional activity of two GM4,6D polypeptides identified as SEQ ID NO:2 and SEQ ID NO:3. Because it discloses both the actual structure and the functional activity of two species of target proteins for the claimed methods of treating a subject having an inflammatory disorder, the skilled artisan would recognize that the specification adequately describes agents (for example, anti-GM4,6D antibodies) that are useful to treat inflammatory disorders characterized by aberrant GM4,6D activity.

Accordingly, Applicants submit that a *prima facie* case of inadequate written description has not been established for claims 21, 23, and 26-29. Likewise, the instant specification reasonably conveys to the skilled artisan those agents that are "capable of inhibiting GM4,6D activity, wherein GM4,6D comprises SEQ ID NO:2 or SEQ ID NO:3" as recited in independent claim 38 and, therefore, a *prima facie* case of lack of adequate written description has not been established for new claims 38-42.

**35 U.S.C. § 112, first paragraph–Enablement**

Claims 21, 23, and 26-29 are rejected under 35 U.S.C. § 112, first paragraph as allegedly non-enabled. The Examiner acknowledges that the specification is "enabling for a method of treating a subject with antibodies against the GM4,6D of SEQ ID NO:2 and 3." (Office Action at page 4.) The Examiner contends, however, that the specification "does not reasonably provide enablement for the treatment of a subject with any modulators against GM4,6D or antibodies against GM4,6D different from SEQ ID NO:2 and 3." (*Id.*)

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The test of enablement is whether one skilled in the art could make or use the claimed invention from the disclosures in the patent application coupled with information known in the art without undue experimentation. *United States v. Telectronics, Inc.*, 8 U.S.P.Q.2d 1217, 1222 (Fed. Cir. 1988). A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner,* 18 U.S.P.Q.2d 1331,1332 (Fed. Cir. 1991). Determining enablement is a question of law based on underlying factual findings. *In re Vaeck*, 20 U.S.P.Q.2d 1438, 1444 (Fed. Cir. 1991). The law allows some reasonable experimentation, and does not require Applicants to disclose each embodiment of the claimed invention. Enablement "is not precluded even if some experimentation is necessary, although the amount of experimentation needed must not be unduly excessive." *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 94 (Fed. Cir. 1986). Additionally,

> [a] specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which corresponds in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. §112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

M.P.E.P. § 2164.04. The Examiner has the initial burden of establishing a reasonable basis to question the enablement provided for the claimed invention. M.P.E.P. § 2164.04; *see also In re Wright*, 27 U.S.P.Q.2d 1510, 1513 (Fed. Cir. 1993).

The Examiner has the initial burden to show, supported by the record as a whole, why the specification is not enabling. *In re Angstadt, supra*. In the present case, the

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Examiner has not met this burden. Although, the Examiner may have demonstrated that some experimentation may be required to practice the claimed methods necessary, doing so is not enough to shift the burden to Applicants to prove that such experimentation is not undue.

First, the term "GM4,6D activity" is clearly defined in the specification as "the ability to convert GDP-mannose to GDP-4-keto-manose" (see page 5, line 12). Second, the specification provides the following screening assay to identify compounds that inhibit GM4,6D activity:

> a first mixture is formed by combining a GM4,6D peptide of the present invention with GDP-mannose by such peptide, and the amount of conversion in the first mixture ($B_0$) is measured. A second mixture is also formed by combining the peptide, the substrate and the compound or agent to be screened, and the amount of conversion in the second mixture (B) is measured. The amounts of conversion in the first and second mixtures are compared, for example, by performing a $B/B_0$ calculation. A compound or agent is considered to be capable of inhibiting enzyme activity if a decrease in conversion in the second mixture as compared to the first mixture is observed.

(See page 8, lines 20-28.)

Third, Example 2 provides the three additional assays for measuring GM4,6D activity. Thus, the Applicants teach that inhibitors useful in the claimed methods of modulating GM4,6D activity may be also be identified by observing GM4,6D activity by:

> (1) incubation of radiolabeled $^{14}C$ or $^{3}H$ on unlabeled GDP-mannose in the presence of salts, buffers and cofactors with enzyme or enzyme extracts, and separation of the reactants and products by HPLC (for example, as described in Yamamoto et al. (1993) Archives of Biochemistry and Biophysics, vol. 300, 694-698) (See page 12, lines 27-31.);

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> (2) coupling the reaction with the enzyme(s) GDP-4-keto-6-deoxy-mannose, epimerase, reductae [*sic*] and monitoring the coupled oxidation of NADPH using, for example, visible or fluorescent spectroscopy (for example, as described in Yamamoto et al., supra). (See page 12, line 31 - page 13, line 4.); or
>
> (3) following the absorbance of the product GDP-4-keto-6-deoxy-mannose at 325 nm in alkali solution (for example, as described by Kornfled and Ginsberg (1966) Biochimica et Biophysica Acta, vol. 117, 79-87). (See page 13, lines 5-7.)

Thus, it would only be a matter of routine experiment to identify GM4,6D modulators for use in the claimed methods. In view of the Applicants' teachings, the specification does enable the claimed methods for treating a subject having an inflammatory disorder characterized by aberrant GM4,6D activity or aberrant GM4,6D nucleic acid expression. Accordingly, Applicants submit that all of the pending claims are properly enabled by the instant specification.

**35 U.S.C. § 112, second paragraph**

Claims 21, 23, and 26-29 are rejected under 35 U.S.C. § 112, second paragraph as being indefinite. According to the Examiner, the "mere recitation of the name 'GM4,6D' is insufficient to convey with clarity that which the Applicant sees as the invention." (Office Action at page 6.)

The instant specification does much more than merely reciting the name GM4,6D. The specification describe two representative species by actual chemical structure and further provides multiple assays for GM4,6D activity, as discussed in

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detail above. Accordingly, claims 21, 23, and 26-29 particularly point out and distinctly claim the subject matter which applicants regard as their invention.

Likewise, this indefiniteness rejection is inapplicable to new claims 38-42, which specifically require that the methods of the invention be practiced with inhibitors that are "capable of inhibiting the GM4,6D activity of a polypeptide comprising the amino acid sequence of either SEQ ID NO:2 or SEQ ID NO:3."

Accordingly, Applicants submit that each of pending claims 21, 23, 26-29, and 38-42, complies with the requirements of 35 U.S.C. § 112, 2nd paragraph.

## Conclusion

In view of the foregoing amendments and remarks, Applicant respectfully requests the reconsideration and reexamination of this application and the timely allowance of the pending claims. Should the Examiner not believe that the claims are in conditions for allowance, Applicants request that the Examiner contact the undersigned representative at (617) 452-1643 for an interview to discuss the application.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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Dated: August 22, 2003

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